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Recent Concept, Patho - Physiology, Diagnosis and Comprehensive Management of Post Herpetic Neuralgia in Day to Day Practice of Stomatology: A Review Article

Lt Col (Dr) I Mukhopadhyaya (Retd)[1], Dr Vaibhava Raaj[2], Dr Camelia Saha[3], Dr Sakshi Raina[4], Dr Khushboo[5], Dr Romshi Raina[6]

[1]Sr Consultant Oral – Dental Surgeon, Apollo Clinic Thakurpukur, Kolkata, WB

[2]Oral – Dental surgeon, ECHS Polyclinic, Ara, Bihar

[3]Consultant oral - dental surgeon, Apollo Clinic Thakurpukur, Kolkata, WB

[4]Oral - Dental surgeon, ECHS Polyclinic Samastipur, Bihar

[5]District Technical Officer, Homi Bhabha Cancer Hospital & Research Centre, Muzaffarpur

[6]Research Officer, National Resource Centre for Oral Health And Tobacco Cessation, Maulana Azad Institute of Dental Sciences, New Delhi

Abstract: ***Post herpetic neuralgia, a chronic neuropathic pain disorders that may occur in the region of Herpetic rashes (HZ), persisting even after the complete remission of skin or oral mucosal lesions. Though there is a huge advancement in diagnostics and current therapeutic avenues, still many patients remain susceptible to physical, psychological & economical distress. Moreover, in orofacial region specially, patients present various overlapping pain as if they are of odontogenic in nature. Patient may experience various types of pains, ranging from hyperalgesia (painful stimuli experienced more painful than expected), allodynia (pain associated with typical nonpainful stimuli) etc. Through history of present and past illness of patient, careful examination and complete utilization of all modern diagnostic facilities not only help the treating surgeon to identify and eradicate the primary cause, but also help us to begin early treatment of the neuralgic pain, thereby increase in satisfaction as well as confidence of patients to many folds.***

Keywords: Neuralgia, Herpes Zoster, Hyperalgesia, Allodynia

1. Introduction

Herpes Zoster, also known as *Shingles* actually derived from Latin word '*Cingulum*', which means 'Belt', is defined as a vesiculo - bullous muco - cutaneous lesion due to reactivation of the *Varicella zoster* virus in sensory neurons or at their ganglions. The acute and classical herpetiform vesicles of muco - cutaneous distribution can be diagnostic when the vesicles are segmental in distribution, unilateral in involvement and presented with symptoms like pain and burning sensation, along with fever, headache, myalgea, joint pain, anorexia as prodormal symptom. HZ involves mainly thoracic (53%), Cervical (20%), Opthalmic (5%), lumbo - sacaeral (11%) unilaterally, where are bilateral is extremely rare (1). In very recent studies it has been found out that the pain associated with HZ is of three phases, an acute phase of herpetic neuralgeal (which last for 30days after onset of rashes), subacute phase that last for (30 - 120days after the onset of rash) and post herpetic neuralgea, where pain persist even after 120 days of onset of skin or mucosal rashes/vesicles (4). There is a variation of patient also surprising on 50% of the affected individuals recover within a year of onset of the pain, where as rest may have for a prolonged duration (4). The disorder follows a classical dermatomal distribution of the rashes as caused by the virus. Unilateral thorasic dermatomes and Trigeminal nerve (specially C1 division) mainly seen to be affected in neuralgea (4). Though the actual reason is still obscure why the other branches of Trigeminal nerve are less affected. The typical Neuralgic pain is described as sharp lancinating or electric shock like sensation, other than patchy allodynia, hyperesthesia and hypoesthesia.

Pathophysiology of Herpes Zoster and PHN: Varicella Zoster is a highly contagious, double stranded DNA virus, responsible for primary manifestation of Chicken Pox in a non - immune or incompletely immune sensitized individual. During this primary infection the virus gets its entry to the sensory dorsal root ganglia.

Pathophysiology of PHN involves disturbances within the central and peripheral nerve. During the acute illness phase of HZ the dormant virus reactivated and replicates to propagate along the affected nerve. This result in triggering of an inflammatory immune response which is capable to damage the peripheral and central neurons (2, 20). The newly synthesized virus particles undergo axonal transport along the course of central and distal axons of the respective sensory nerves (from affected dermatomes). As a result there is a generalized necrosis and cell death of the skin as well as within the nerve root and their ganglions (2, 21). The damaged peripheral nerves loose their ability to function

properly in form of inhibition of nociception pain signals, which results in lowering down of threshold of nociceptive pain activation. On the other hand, this malfunction of inflammed nerves leads to production of spontaneous ectopic discharges. This finally results in generation of disproportionate pain even with nonpainful stimuli, a phenomenon know as *Peripheral Sensitization*. HZ virus induced inflammatory condition of nerve impares descending inhibitory pain pathways, which is secondary to compromisation of dorsal horns and ultimately leads to central sensitization (2). This phenomenon to some extent clearly describe the spontaneous pain in PHN due to changes induce an abnormal reorganization of pain stimuli transmission system and disorganization of pain stimuli transmission system leading to disorganization of innervation patterns as a result of death of peripheral neurons and changes in central nervous system. (2)

PHN does not restricts its mechanism at peripheral or central neurons, but also at the cellular level, it up - regulates the receptor typically associated with pain, like "Transient Receptor Potential Vanilloid" (TRPV) and cause in increase in the proportion of voltage gated sodium channels and potassium channels (2, 23). In various studies it has been evident that there is loss of (gamma) - aminobutaric acid inhibitory interneurons at the dorsal horn in addition to loss of descending inhibition (2, 22). Watson et al. compared an atopy tissue from patients with and without PHN after HZV infection, showed that patient with PHN had more degeneration than the non PHN patients spinal cord dorsal horn. However it again remains obscure that the dorsal horn atrophy is actually a sequeally of direct infection of spinal cord or by trans synaptic degeneration (2, 24). Though there is a predilection of involvement of sensory nerve and ganglia, motor neurons involvement may occur from spread of infection and inflammation to the anterior horn of spinal cord (2, 25), which may lead to development of signs of motor nerve compromisation as well as pain that is sensory involvement.

The Neuralgea has been subdivided into two broad models, the irritable nociceptor and de - afferentiation modes (2/26). The former model presents as severe allodynia by mechanical, thermal and tactile stimulation with minimal loss of sensory sensation and the same is conducted with 'C' fibers predominantly and actively. Generally, ‘C’ fibers are stimulated by noxious stimuli, but with molecular changes the ‘C’ fibers become sensitized, by lowering their threshold of action potentials. The ultimate result of this stimulus is PNS mediated spontaneous pain and allodynia. De - afferentiation is associated with allodynia as well as sensory loss at the involved dermatomes, which results reorganization of dorsal horns and quantitative diminish of C fibers in the affected area. Various studies showed loss of epidermal free nerve ending significantly in skin biopsy of the affected area. This results in sprouting of A - B (beta).

Diagnosis of PHN

A positive history of post HZ infection and the nature of pain are of paramount importance as they are the critical parameters for diagnosis of PHN. For a practicing stomatologist or dental surgeon, it's very important to get details of past and present medical history, history of *vaccination* and the symptoms along with a careful physical examination which can assess the pain and its impact on day to day life of a patient. Detailed examination can reveal, areas previously affected by HZ may by the cutaneous scanning and rashes for site of pain by thorough inspection. One has to look into the changes of skin color and presence of edema to differentiate from other inflammation. Areas of sensory abnormality like allodynia, hyperalgesia or dysesthesia in the affected site required to be assessed by sensitivity with touch (like light touch with cotton roll or swab or by paint brush or pin prick with needle/safety pin or toothpick) for thermal response to warm or cold stimulus (like by metal thermorollers) or for the response to vibration (by using a 128 HZ tuning fork), that can be very much helpful for the framing of proper comprehensive treatment plan. Pain sensitivity, intensity and magnitude should be assessed by using an appropriate pain scale based on patient's education, socio - economic status and ability to communicate with the doctor. Generally, we can choose a numerical rating scale (0 - 10, a 11 point scale where 0= no pain and 10= extremely severe pain), a visual analog scale or a verbal descriptor scale (like Mc Gill pain questionnaire) for the successful outcome of treatment of PHN. It is very much important to evaluate the quality of the life that, patient is living or has been impaired due to Neuralgia.

Management of PHN

Treatment of PHN does not only exist the treatment of Neuralgia, that the patient is suffering but it includes prevention of occurrence of HZ infection, by proper vaccination. It has been seen that PHN has been found in elderly age groups relatively sparing the younger age, as the prevalence of HZ is less common in young generation. The best way to prevent PHN is to ensure vaccination with VZV, and there by avoid infection. In a study it has found, the prevalence of VZV/PHN is less in those children who has been inoculated with *chicken pox* vaccine after its induction. But those adults who had the history of VZV infection in childhood and therefore there remains a possibility of latent HZ infection, can be prevented by proper vaccination of live attenuated *shingles vaccine*. Various studies has been shown the effectiveness of vaccination while reducing the incidence of HZ and thereby development of future PHN to a great extent. Earliest treatment (with 48hrs) with oral or parentaral antivirals in case of HZV showed reduction of viral load in dorsal root ganglia, thus it has been seen to reduce the incidence and severity of PHN in the affected persons.

Tricyclic antidepressants drugs - TCA, are class of drugs primarily designed to treat various mood alterations, depression and also to manage the various chronic pains. They are second line drug next to selective serotonin reuptake inhibitors (SSRI). TCA are discovered in early 1950s but marked later. They are named so as they are of three rings of atoms. Although TCA are prescribed for various mood depression but have been largely replaced by newer antidepressants like (SSRIs) (6), Serotonin nor - epinephrine reuptake inhibitors (SNRIs) and nor - epinephrine reuptake inhibitors (NRIs). The TCAs are primarily designed for the treatment of various mood disorders such as (MDD), dysthymia, and various resistant variants. They are still a popular drug for various medical conditions like anxiety disorders, OCD, PD, BPD, ADHD,

IBS, IC, NE, Chronic hiccups, as an adjunct in schizophrenia and many more. But TCAs are also used widely in Chronic Neuropathic pain, migrane prophylaxis, chronic tension headache, and neuralgea/fibromyalgia. The precise mechanism of action is unclear, but is thought to be due to modulation of Opoid system in brain and downstrim via serotonergic or nor adrenergic neuro modulation. There are few side effects are there which we should be aware of, mainly due to a anti - mascarinic property, like dry mouth, dry nose, blurring of vission, lower gastrointestinal motility, and constipation and urinary retention, cognitive and memory imparement as well as increased body temperature, other minor side effects are drowsiness, anxiety, emotional blunting (apathy), confusion, restlessness, changes of appetite and weight gain, tachycardia, rarely irregular heart beat. Rabdomyolysis or smooth muscle breakdown also reported as rare side effects. Antidepressants may produce withdrawal, hence 'discontinuation syndrome' can be well managed by gradual withdrawal of drug over a period of weeks or months. TCAs overdoses may cause fatal drug personing with high morbidity or mortality due to cardiovascular tachycardia, hypotension or thostaris, arrhythmias) CMS (syncope, seizure, hyperreflexia, coma), pulmonary effects (hyperventilation leading to CNS depression), GI (decrease or absence of bowel movements). TCAs are highly metabolised in liver in presence of cytochrome P450, thereby antagonist like calcium channel blockers, other anti - psychotics in tract the metabolism.

Pregabolin: Pregabolin, (S) - 3 - (aminomethyl) - 5 - methyl hexanoic acid in pharmacologically active element of 3 - iso butyl Gamma amino butyric acid analogue. This drug is an antagonist of Voltage Calcium channel and specifically binds to alpha - 2 - delta subunit to produce it effective anti - epileptic as well as analgesic effects, thus to reduce various types of Neuropathic pain like allodynia or hyperalgesia, fibromyalgia, PHN with economically great tolerance in all the age group, as mono therapy or as combined drug with other drugs. It has been seen in various studies that pregabolin when administered 10mg/kg to 30mg/kg orally for 8days, reduce the neuropathic pain significantly along with reduction of substance P, CGRP (Calcitonin Gene - Related Peptides), though it is recommended to give 150 - 160mg/day for 8 - 13 weeks to resolve the PHN with mild to moderate dizziness. The drug is very well tolerated by all age group but their few side effects as listed are to be taken care off, like dizziness, somnolence, headache, dry mouth, peripheral edema, weight gain, blurring of vision (1 - 10%) in lower doses. The intensity of the effects increased with doses. Apart from these effects a few number of patient (<1%) may develop CVS abnormality who were already having it.

Gabapentin: Gabapentin belongs to the class of drugs that is known as anticonvulsants. But it can be used in post Herpetic Neuralgea to manage the pain of damaged nerve caused by *Shingles*. We can achieve an optimal result if we go for a combination therapy. The exact mechanism of action is not fully clear to us but it seems to act by preventing the increase in sensitivity to pain in post Herpetic Neuralgia.

Though this medicine is very well tolerated when given orally but a mild to severe side effects are listed in few cases. Most common side effects are like increase susceptibility to viral infection, fever, nausea, vomiting, hostility, jerky movements of extremities etc. These are common in pediatric age groups. Some serious side effects are like change of mood or increase anxiety (thoughts of suicide or dying, restlessness, panic attacks, trouble sleeping, unusual mood or behavior change) changes in behavior like trouble in concentrations, aggressiveness, restlessness, hyperactive behavior etc.

Sometimes serious allergic reactions has also been noted, with different degrees of complications and manifestation. A few drug interactions has been noted with Gabapentin when they are taken orally, like with morphine, antacids containing aluminum hydroxide or magnesium hydroxide, alcohol.

Doses: Maximum permissible dose in a healthy adult per day in 1800mg (600mg, three times a day). The oral preparation may be started as 300mg/day and can be increase by 900mg/day depending upon the improvement.

Some condition are contraindicated for prescribing the drugs like, patient suffering with chronic kidney disease (CKD), for pregnant women, women with history of breast - feeding and children below 3years.

Capsaicin Cream: - Capsiacin cream or patch can potentially improve the pain condition of a PHN patient when it is used regularly at least for 3 months. They basically act by down regulating the TRPV1 receptor and blocking the substance P, a natural algogenic substance. In some cases it has been seen, application of topical cream of capsaicin has eliminate the use of TCAs and anticonvulsants like Pregabolin or Gabapentin. As topical capsaicin is able to provide efficient pain relief with a little central nervous system effects and a minimal drug regimen border.

2. Conclusion

Discussion

Post herpetic neuralgia (PHN) is one of the most resistant type and chronic pain disorder, affecting not only patients of old ages but also the middle aged young adults are being seen suffering. It is being presented as a pain that persists even after the complete resolution of the skin and mucosal rashes caused by the virus. Although a variety of definitions of PHN have been given by clinicians and researchers, the results of recent studies suggest that the pain associated with herpes zoster has three phases: *an acute herpetic neuralgia*, where the pain that accompanies the rash lasts up to 30 days after the onset of rashes; *subacute herpetic neuralgia* that lasts for 30 – 120 days after the onset of rashes; and *post - herpetic neuralgia*, where the pain persists beyond 120 days after the onset of rash. The duration of PHN is extremely variable and approximately about 50% of the patients recover within a year of onset of pain.

Sequential and combination treatments, with first and second - line medications, can be used to enhance pain relief and achieve improvement in the quality - of - life of all affected

individuals. An ideal treatment would involve '*rational polypharmacy*' based on the understanding of the pathophysiological mechanisms of herpes, and such an approach to the treatment of post - herpetic neuralgia may become possible, as the understanding of the mechanisms of pain increase. However, there is no data regarding the additive or synergistic benefits of combination treatment, and it is not known which patients are most likely to be benefited from what combinations. Moreover, the disadvantages of such combinations include an increased risk of side effects due to the simultaneous use of a multiple class of drugs and the difficulty in identifying which medication caused that adverse effect. Apart from drugs, various non - pharmacological therapies are also added to enhance the pain relief by controlling the physiological and psychological components of pain. These therapies can be in the form of TENS, behavioral therapies and psychological counseling. Although there are no proper randomized controlled trials to support them, the lack of any significant side effects and cost - effectiveness has been supporting them since decades

Local applications of various drugs have an advantages over systemic analgesics, as they have a potential to decrease pain without significant side effects. These preparations are mostly effective when the subjects have thermal and mechanical allodynia.

Capsaicin (trans - 8 - methyl - N - vanillyl - 6 - nonenamide) is a selective blocker for the receptor potential vanilloid 1 receptor (TRPV1). The very primary effect of capsaicin is the activation of the TRPV1 - expressing cutaneous nociceptors, which result in pungency and erythema due to the release of vasoactive neuropeptides. **Capsaicin - activated the cutaneous nociceptors are reversible and it has been seen that normal function (the detection of noxious sensations) returns within weeks in healthy volunteers.** Three different concentrations of this drug have been studied and used,

a) Capsaicin cream (8%)
b) Capsaicin cream (0.075%)
c) Capsaicin (0.025%)

Several studie has been shown that at a lower concentration of capsaicin (0.025%) is also to be effective, although two or more weeks of treatment may be required to get the full benefit of the cream.

Treatment with the *lidocaine patch 5%* consists of the application of a maximum of three patches per day for a maximum of 12 hours, applied directly to the area of maximal PHN - associated pain and allodynia. Various studies concluded that patients with varying degree of allodynia obtained significant relief and the side effects were found to be only mild skin reactions like erythema and rash of local areas. Considering the proven efficacy and safety profile, the lidocaine patch 5% is still being used as a fi rst - line therapy for the treatment of this type neuropathic pain. Topical nonsteroidal anti - Inflammatory drugs like topical aspirin has also been studied by various researchers with variable response and are not advocated for regular uses.

Interventional therapies in some patients with refractory pain of PHN may have shown poor control with all conventional single or combination multidrug therapy can be selectively chosen for using epidural injections, para vertebral nerve blocks, sympathetic nerve blocks, intrathecal steroids, and pulsed radiofrequency. Epidural injection of a local anesthetic agents when choosne for either intermittently or continuous catheterisation in severely painful cases of acute or refractory in nature is found to be effective in reducing pain severity and duration. Paravertebral nerve block has been used to relieve pain in PHN using multiple doses injections with repeatation of local anesthetic mixture (Bupivacaine 0.5% and clonidine) every 48 hours for three weeks, using a catheter inserted at the T2 - T3 level, but evidence to support this treatment is not very encouraging. Various intraspinal agents such as opioids and local anesthetics agents have been used with varying degree success, especially when administering the local anesthetics as adjunctive this agents to the level of the segmental block. Radiofrequency ablation using the heat lesioning has been reported in a few journals with complications dysesthesias, hypesthesias, proprioceptive losses, paresis etc in the deafferentation of pain resulting from post - herpetic neuralgia. . Pulsed radiofrequency lesioning (PRF) is relatively a safe, nondestructive, neuroablative modality of lesioning. It helps in pain modulation and can be performed multiple times, as needed though mode of action is not very much clear but has been postulated to modulate the pain processing mechanisms at the dorsal root ganglion, dorsal horn, and molecular levels. There was excellent pain relief (about 55%) at four weeks, with the effect.

Various surgical modalities such as ablative therapies, like neurolytic nerve blocks, peripheral neurectomy, dorsal root entry zone lesions, sympathectomy, trans - spinal ganglionectomy, prefrontal lobotomy has been tried in patients refractory to all the conventional treatments.

Recent advancement with the newer antidepressant drugs such as, venlafaxine, bupropion, and paroxetine those who are having analgesic properties but the overall eff ectiveness of these drugs is probably less than the tricyclic antidepressants, but with less side effects. Patients who are predisposed to tricyclic side effects, or who have not been able to tolerate these drugs, may be considered for the trials with these agents of the newer antidepressants.

3. Future Research

1) Control and prevention of herpes zoster infections by effective mass vaccination and thus eradication of the disease from the community will be the goal.
2) Our second aim should be prevention of post - herpetic neuralgia in those individuals who will be affected with herpes zoster
3) Research to be carried out to Identify the very of subtypes based on the pathophysiology of post - herpetic neuralgia will hold a key to the successful treatment
4) Ongoing and future clinical research is expected to defi ne the effi cacy of all the above discussed therapies and outline a treatment protocol that may help us to make a comprehensive approach tailored to each patient.

5) There is definite need to study the role of invasive pain management techniques in the treatment of PHN with refractory pain.

References

[1] Simant Ankit, Tongxiang Zeng*, Yangxin Chen, Hari Narayan Gupta, Kunal Shah, Xianwang Wang, The Current Treatment and Prevention of Post Herpetic Neuralgia, Scientific Resarch Publishing, 2018, 28 - 38
[2] Graham R. Hadley. Julie A Gayle, Juan Ripoll, Mark R. Jones, Charles E. Argoff, Rachel J. kaye, Post - herpetic Neuralgia: a Review, Springer, (2016) 17 - 21
[3] Julia Forstenpointner, Andrew SC Rice, Nanna B. Finnerup and Ralf Baron, Up - date on Clinical Management of Postherpetic Neuralgia and Mechanism - Based Treatment: New Options, The Journal of Infectious Diseases (Suppl2), S120 - S126
[4] Saru Singh, Ruchi Gupta, Sukhdeep Kaur, Jasleen Kaur, Post - herpetic neuralgia: A review of current management strategies, Indian Journal of Pain, January - April 2013, Vol27, Issue 1, 12 - 21
[5] Theresa Mallick - Searle, Brett Snodgrass, Jeannine M Brant, Postherpetic neuralgia: epidemiology, pathophysiology, and pain management pharmacology, Journal of Multidiscipliary Healthcare, 2016; 9, 447 - 454
[6] Dworkin RH, Schmader KE. Treatment and prevention of postherpetic neuralgia. Clin Infect Dis 2003; 36: 877 - 2.
[7] De Benedittis G, Besana F, Lorenzetti A. A new topical treatment for acute herpetic neuralgia and post herpetic neuralgia: The aspirin/diethyl ether mixture. An open - label study plus a doubleblind controlled clinical trial. Pain 1992; 48: 383 - 90.
[8] Chen N, Li Q, Zhang Y, Zhou M, Zhou D, He L. Vaccination for preventing postherpetic neuralgia. Cochrane Database Syst Rev 2011; 3: CD007795
[9] Upadhyay SP, Rana SP, Mishra S, Bhatnagar S. Successful treatment of an intractable Postherpetic Neuralgia (PHN) Using Peripheral Nerve Field Stimulation (PNFS). Am J Hosp Palliat Care 2010; 27: 59 - 62
[10] American Academy of Neurology. Neurology 2004; 63: 959 - 65.29. Kuthuru MR, Kabbara AI, Boswell MV. Pulsed radiofrequency ablation of frontal and supraorbital nerves for postherpetic neuralgia: A case report. Reg Anesth Pain Med 2003; 28: A56
[11] Woolf CJ, Mannion RJ. Neuropathic pain: aetiology, symptoms, mechanisms, and management. Lancet.1999; 353 (9168): 1959–19
[12] Irving G, Jensen M, Cramer M, et al. Efficacy and tolerability of gastric - retentive gabapentin for the treatment of postherpetic neuralgia: results of a double - blind, randomized, placebo - controlled clinical trial. Clin J Pain 2009; 25: 185–92.
[13] Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus - Miller L. Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial. JAMA 1998; 280: 1837–42.
[14] Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta - analysis. Lancet Neurol 2015; 14: 162–73. . Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta - analysis. Lancet Neurol 2015; 14: 162–73.
[15] Daniel HC, Narewska J, Serpell M, Hoggart B, Johnson R, Rice AS. Comparison of psychological and physical function in neuropathic pain and nociceptive pain: implications for cognitive behavioral pain management programs. Eur J Pain 2008; 12: 731–41
[16] Webster LR, Malan TP, Tuchman MM, Mollen MD, Tobias JK, Vanhove GF. A multicenter, randomized, double - blind, controlled dose finding study of NGX4010, a high - concentration capsaicin patch, for the treatment of postherpetic neuralgia. J Pain 2010; 11: 972–82.
[17] Watson CP, Tyler KL, Bickers DR, Millikan LE, Smith S, Coleman E. A randomized vehicle - controlled trial of topical capsaicin in the treatment of postherpetic neuralgia. Clin Ther 1993; 15: 510–26.
[18] Bernstein JE, Korman NJ, Bickers DR, Dahl MV, Millikan LE. Topical capsaicin treatment of chronic postherpetic neuralgia. J Am Acad Dermatol 1989; 21: 265–70
[19] Watson, P. N. (2010) Postherpetic Neuralgia. BMJ Clinical Evidence, 2010, Article ID: 0905.
[20] Argoff CE, Katz N, Backonja M. Treatment of postherpetic neuralgia: a review of therapeutic options. J Pain Symptom Manag.2004; 28 (4): 396–411.
[21] Head H, Campbell A. The pathology of herpes zoster and its bearing on sensory localisation. Brain.1900; 23: 353–532.
[22] Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms and treatment. Lancet Neurol.2010; 9 (8): 807–19.
[23] Garry EM, Delaney A, Anderson HA, et al. Varicella zoster virus induces neuropathic changes in rat dorsal root ganglia and behavioral reflex sensitization that is attenuated by gabapentin or sodium channel blocking drugs. Pain.2005; 118 (1–2): 97–111.
[24] Dastidar P, Haanpää M, Weinberg A, Levin M, Miettinen A, Lapinlampi A, et al. CSF and MRI findings in patients with acute herpes zoster. Neurology.1998; 51: 1405–11.
[25] Opstelten W, McElhaney J, Weinberger B, Oaklander AL, Johnson R. The impact of varicella zoster virus: chronic pain. J Clin Virol.2010; 48: S8–S13.
[26] Fields H, Rowbotham M, Baron R. Postherpetic neuralgia: irritable nociceptors and deafferentation. Neurobiol Dis.1998; 5 (4): 209–27.